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(19)(CA) **APPLICATION FOR CANADIAN PATENT** (12)

(54) Hot Flu Composition

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ABSTRACT

A composition useful for the treatment of cold and flu symptoms and associated discomfort, composed of an analgesic, preferably Acetaminophen, an antihistamine, an antitussive, decongestant, citric acid, a bicarbonate, calcium carbonate, flavors and sweetners, tablet lubricants and other tableting aids. The composition is dissloved in hot water prior to ingestion and provides a palatable solution.

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HOT FLU COMPOSITION

Field of the invention

The field of the invention is a composition intended for dissolution in hot water prior to ingestion. The composition is provided in the form of a tablet and contains multiple ingredients including an analgesic, an antihistamine, a decongestant and an expectorant making it suitable for use with symptoms commonly referred to as flu symptoms.

Background of the invention

There are many cold products on the market containing multiple ingredients. US Patent No. 4,975,426 discloses a cough/cold mixture containing a nonsedating antihistamine, an analgesic chosen from the group consisting of aspirin, sodium salicylate, salicylamide or acetaminophen, and optionally one or more other active components selected from a decongestant, cough suppressant (antitussive) or expectorant for the relief of cough, cold, cold-like and or flu symptoms and the

discomfort, pain, headache, fever and general malaise associated therewith.

EP 418564, commonly assigned herein, discloses a low sodium effervescent cold or sinus allergy medicine composition. This composition is provided as an effervescent tablet and is dissolved in cold water prior to ingestion. The composition disclosed has a reduced sodium content and comprises: 0.2 to 16 % acetylsalicylic acid, acetaminophen, ketoprofen or mixtures thereof as the analgesic; 24 to 38% citric acid; 12 to 19 % sodium bicarbonate as the only sodium containing active ingredient; 8 to 13 % calcium carbonate; 9 to 14 % potassium bicarbonate; 0.05 to 0.1 % antihistamine; 0.1 to 1.2 % decongestant; 0 to 0.6 % antitussive; 0 to 11% glycine; 0.8 to 1.3 % flavors and sweetners; 0 - 33 % tableting aids other than lubricants and 0 to 6% tablet lubricant other than acetylsalicylic acid. Such percentages are weight percentages pased on the total composition.

TheraFlu® is marketed as a powder packet by Sandoz as a flu and cold medicine and is intended for dissolution in hot water prior to ingestion. According to the Physician's Desk Reference for Nonprescription Drugs. It contains 500mg Acetaminophen, 60mg Pseudoephedrine Hydrochloride, 4 mg Chlorpheniramine Maleate, and 20 mg Dextromethorphan Hydrobromide as active ingredients, and in addition, it contains ascorbic acid, citric acid, natural lemon flavors, sodium citrate, sucrose, titanium dioxide, tribasic

calcium phosphate, pregelatinized starch, Yellow 6 and Yellow 10.

None of the prior art disclosures specifically disclose or suggest the novel compositions of the present invention.

Summary of the Invention

This invention compositions may be provided in the form of an effervescent tablet for dissolution in hot water prior to ingestion, referred to as a hot flu preparation, for cough, cold, cold-like and flu symptoms and associated discomfort. The composition includes an analgesic chosen from the group consisting of Acetaminophen, acetylsalicylic acid, ketoprofen and ibuprofen, a decongestant, an antihistamine and an antitussive. Acetaminophen is a preferred analgesic.

A hot flu compositions comprise:

a. 0.9 to 17 % weight percent of an analgesic chosen from the group consisting of acetaminophen, acetylsalicylic acid, ketoprofen and ibuprophen;

b. 0.07 to 0.14% antihistamine;

c. 0.4 to 1.2% antitussive;

d. 1 to 2% decongestant;

e. 10 to 20% citric acid;

f. 1.5 to 2.2% sodium or potassium bicarbonate;

g. 1.5 to 3% calcium carbonate;

h. 2 to 4% flavors and sweetners;

i. 1.5 to 2.5% tablet lubricants; and

j. the remainder as tableting aids other than tablet lubricants.

Detailed description of the Preferred Embodiment

It was desirable to produce an effervescent tablet form which could be dissolved in hot water to provide a hot drink flu and cold preparation. Although the effervescent cold or sinus allergy medicine composition described previously contained active ingredients similar to those desired in such a product, an analgesic, a decongestant, an antitussive and an antihistamine, it was found that the previous composition could not be dissolved in hot water without causing a possibly dangerous rapid effervescent reaction during which the solution formed could overflow the container. In addition, many analgesics including ibuprofen, ketoprofen and acetaminophen have a particularly bitter taste which appeared to be accentuated by the hot drink formulation. Therefore, there was a need to develope a new tablet formulation for an analgesic, an antihistamine, a decongestant and an antitussive which could be dissolved in hot water prior to ingestion for symptoms of cold and flu.

It was found that the content of bicarbonate in the formulation must be reduced and that calcium carbonate would mask the bitter taste of acetaminophen. When used a low levels as in the formulation disclosed, the chalky taste of the calcium carbonate helps to mask the bitter taste of acetaminophen. If used in greater amounts, calcium carbonate should be employed in an amount to

provide a total daily dosage not exceeding 8 gm. The calcium carbonate is preferably employed in the spray-dried form described in US Patent No. 4,650,669. It was found that while potassium or sodium bicarbonate could be used, a low level of sodium bicarbonate provided a sufficient solubility aid in hot water. If potassium bicarbonate is employed, the amount should not exceed a total daily dose of 2.4 gm. However, palatability of the dissolved solution is improved if potassium bicarbonate is avoided. It was not necessary to use glycine to increase the acid neutralizing capacity of the composition. The resulting formulation when dissolved in water produces a pH of from about 2.2 to about 2.5.

The product also contains one or more antihistamines, such as chlorpheniramine maleate, brompheniramine maleate and pyrilamine maleate as well as one or more decongestants, such as phenylpropanolamine tartrate or bitartrate, phenylephrine bitartrate, and pseudoephedrine sulfate or the corresponding hydrochloride salts. The product may also contain an antitussive, such as dextromethorphan hydrobromide.

The taste of the product after it is dissolved in water can be improved by including in the composition, minor amounts of flavors, such as lemon, grapefruit and orange flavors, as well as sweeteners, such as aspartame and calcium or sodium saccharine. The aspartame may be used in the form of granules containing lactose and a nonionic surfactant as described in US Patent No. 4,783,331.

This composition can be used in a powder-granulated form but is preferably used in the form of compressed tablets. In the production of tablets a lubricant is necessary for the tablet dies. Preferred lubricants are fumaric acid, magnesium stearate and mixtures thereof. It is understood, however, that other well-known tablet lubricants, such as adipic acid and sodium benzoate, can also be used. It is also preferable to include tableting aids other than lubricants, such as inert fillers or binders. Examples of such fillers or binders are sorbitol, lactose, mannitol, fructose, sucrose, a cocrystallized mixture of 97% sucrose and 3% modified dextrins or combinations thereof. It is preferred that the major component of the tableting aids other than lubricants be mannitol.

In order to have a substantially completely dissolved product with no scum floating on the liquid surface, minor amounts of polyvinyl pyrrolidone, organopolysiloxane (such as dimethylpolysiloxane), and dioctyl sodium sulfosuccinate surfactant may be included.

A preferred formulation contains 500 mg Acetaminophen, Pseudoephedrine Hydrochloride, Dextromethorphan Hydrobromide, Chlorpheniramine Maleate, Citric acid, Sodium bicarbonate as the only bicarbonate source, artificial sweeteners, flavors and other components capable of providing suitable tableting characteristics such as lubricants.

The final form of the composition is produced by granulating Chlorpheniramine Maleate, Dextromethorphan Hydrobromide and mannitol with starch paste and then dry blending all remaining ingredients. Final tablet forms are produced by feeding the above mixture to a tablet press in a manner known to those skilled in the art.

The following example describes production of tablets of one form of the preferred composition.

Example

The following formulation is one preferred formulation which solved the problems of taste for tablet containing acetaminophen dissolved in hot water.

Weight %	Ingredient
17.86	Acetaminophen
10.71	Citric Acid
1.79	Sodium bicarbonate
1.79	Calcium Carbonate
0.07	Chlorpheniramine Maleate
1.07	Pseudoephedrine Hydrochloride
0.54	Dextromethorphan Hydrobromide
2.72	Flavors and Sweeteners
59.58	Tableting Aids excluding calcium carbonate and lubricants
1.88	Tablet lubricants

This formulation provided a fast dissolving tablet which provides a palatable hot medicinal drink without the conventional use of sugar and without glycine. The tablet may be formulated by granulating the active ingredients and mannitol powder with 6% by weight starch paste in a high shear granulator. The granules are dried at 130 to 140 degrees F for about 18 to 22 hours. The dried granules are sized. A mixture of flavors, artificial sweetener, diluent, tablet lubricant and calcium carbonate is added and blended with the granules. Tableting may be accomplished with conventional equipment commonly used in effervescent tableting. The resulting tablets dissolve in hot water in less than 60 seconds, providing a solution with a palatable taste.

3. A hot flu composition, comprising

a. 17.86% Acetaminophen;
b. 10.71% Citric Acid;
c. 1.79% Sodium bicarbonate;
d. 1.79% Calcium Carbonate;
e. 0.07% Chlorpheniramine Maleate;
f. 1.07% Pseudoephedrine Hydrochloride;
g. 0.54% Dextromethorphan Hydrobromide;
h. 2.72% Flavors and Sweeteners;
i. 1.88% Tablet lubricants; and
j. 59.58% Tableting Aids excluding calcium carbonate and lubricants.

4. The hot flu composition of claim 3 wherein the tablet lubricants are a mixture of fumaric acid and magnesium stearate.

WHAT IS CLAIMED IS:

1. A hot flu composition, comprising:

a. 0.9 to 17 % weight percent of an analgesic chosen from the group consisting of acetaminophen, acetylsalicylic acid, ketoprofen and ibuprophen;

b. 0.07 to 0.14% antihistamine;

c. 0.4 to 1.2% antitussive;

d. 1 to 2% decongestant;

e. 10 to 20% citric acid;

f. 1.5 to 2.2% sodium or potassium bicarbonate;

g. 1.5 to 3% calcium carbonate;

h. 2 to 4% flavors and sweetners;

i. 1.5 to 2.5% tablet lubricants;

j. the remainder as tableting aids other than tablet lubricants.

2. A hot flu composition, comprising

a. 11.0 to 17 % acetaminophen;

b. 0.07 to 0.14% antihistamine;

c. 0.4 to 1% antitussive;

d. 1 to 2% decongestant;

e. 10 to 20% citric acid;

f. 1.5 to 2.2% sodium bicarbonate;

g. 1.5 to 3% calcium carbonate;

h. 2 to 4% flavors and sweetners;

i. 1.5 to 2.5% tablet lubricants, and

j. the remainder as tableting aids other than tablet lubricants.